IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 6 Ver. III (Jun. 2015), PP 94-98
www.iosrjournals.org

High Sensitivity C-Reactive Protein In Patients With Acute Injuries

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Abstract:
Background: *C- reactive protein has been known as a highly sensitive but non-specific marker for acute inflammation. The pattern of CRP response in trauma patients has not been evaluated in our environment.*
Aim: *The aim of the study was to determine the serial serum level of high sensitivity C- reactive protein (h-sCRP) in patients with trauma.*
Methods: *This is a longitudinal study conducted at the University of Benin Teaching Hospital, Benin City, Nigeria. One hundred and twenty patients with traumatic injuries were recruited at the accident and emergency unit of UBTH and 30 apparently healthy individuals as controls. A structured questionnaire was administered to all subjects to obtain demographics, injury type, tissue involvement and interventions. Samples were collected from participants for estimation of h-sCRP on days 1, 3, and 8. hsCRP was analyzed using an ELISA method. Results were analyzed with SPSS 16. P value was set at 0.05.*
Results: *A total of 116 patients and 30 controls completed the study. The most frequent cause of trauma amongst the patients was vehicular crashes 80 (69.0%) followed by gunshot injuries 19 (16.4%). The mean serum h-sCRP of the patients on the first day was (166.7 ± 105.3mg/L) but it peaked on the third day post trauma (373.4 ± 131.2mg/L) and declined on the eighth day to 300.0 ± 156.5mg/L) (P = <0.001).*
Conclusion: *C- reactive protein levels increase in the blood of trauma patients as a result of tissue damage but decreased after the third day following trauma. However, in the presence of infection, the increase was sustained. We therefore recommend that serial quantitative C-reactive protein measurements be done as an adjunct to surgical care in patients with acute injuries.*
Key Words: *C-reactive protein, Trauma, Acute injuries, Benin City*

I. Introduction

C-reactive protein is an acute phase reactant synthesized in the liver. It was first described by Tillet and Francis in 1930[1] as a substance present in the sera of acutely ill patients and able to bind the cell wall c-polysaccharide of Streptococcus pneumonia and agglutinate the organism. In 1941, the substance was shown to be a protein and given the name C-reactive protein (CRP).[1] Several studies have revealed that the risk of heart-attack, stroke and other cardiovascular conditions is directly related to increasing levels of CRP. For many years, CRP has been known as a highly sensitive but non-specific marker for acute inflammation and an indicator of cardiovascular risk.[1] CRP is known to rise to very high levels within 4-6 hours following acute injurious conditions such as trauma, surgery, or infection. Increased serum CRP levels up to several-hundred-fold are not uncommon after severe trauma.[2] Its level may rise in response to trauma such as burns, fractures or surgery.[3]

CRP is known to increase in severe cases of inflammation and infection and drops as inflammation subsides. It can therefore be useful in assessment of severity, metabolic response, prediction of outcome and monitoring response in trauma patients.

Physical trauma is a leading cause of morbidity and mortality in all age groups, and post-traumatic complications including infections which intensify inflammatory response abound.[4] Therefore, a parameter helpful in monitoring inflammatory response and aiding early diagnosis of infections is not only advantageous for early institution of treatment but also reduces morbidity and mortality to a large extent.

It has also been shown that daily quantitative analysis of CRP in blood of trauma patients allowed prognosis of the development of nonbacterial systemic inflammation response, infectious complications and sepsis.

CRP level >40mg/L on the first day (without use of glucocorticoids) suggest a risk of development of infectious complications.[5] Reduction of CRP from the third day is characteristic of a favorable course of trauma.[5] The onset of some infections may not be easily detected, especially if it is occult such as in the brain and the bladder however rising or persistingly high CRP level may indicate complications. This study therefore

aim to determine the serum levels of CRP in trauma patients on the first, third and eight day following trauma and also assess serum CRP in the patients based on the nature of injury, tissue involvement and surgical intervention.

II. Methodology

Study Design: This is a longitudinal study conducted at the University of Benin Teaching Hospital, Benin City, Nigeria.

Study Population: two groups of participants were recruited for this study including 120 patients with traumatic injuries presenting to the accident and emergency unit of UBTH were recruited as the main study population and 30 apparently healthy persons were recruited as controls.

A structured questionnaire was administered to all subjects to obtain demographic parameters, type of injury, tissue involvement and intervention. Blood samples were collected from the patient group on days 1, 3 and 8 of presentation for evaluation of the pattern of CRP response in the study patients.

Inclusion Criteria: Subjects admitted within first 24hrs of injury; Age 16 – 65 years

Exclusion Criteria: Excluded from the study were patients with other medical conditions such as diabetes mellitus, hypertension and any other condition that can generate inflammatory response.

Blood Sample Collection: Five milliliters of venous blood was collected from the antecubital veins and dispensed into plain bottles for CRP estimation. The clotted blood was centrifuged at 2500 rpm for 10minutes and the serum was separated into clean plain bottles and stored at -20°C and analyzed within 2weeks of collection.

hsCRP Assay: The high sensitivity C-reactive protein (hsCRP) ELISA is based on the principle of a solid phase enzyme linked immunosorbent assay.[6] The assay system utilizes a unique monoclonal antibody directed against a distinct antigenic determinant on the CRP molecule.

Assay Characteristics: Assay was linear up to 10mg/L CRP. Acceptable coefficient of variation (CV) was 20%. A standard of 10mg/L was analyzed in triplicates and the mean was found to be 10mg/L. The bias was zero, giving an accuracy of 100%. A precision control of 50mg/L was analyzed ten times and the mean was 49.5%, standard deviation was 1.3 and coefficient of variation was 2.6%. Hence precision was 97.4%. Serum samples demonstrating gross lipaemia, gross haemolysis or turbidity were not used with this test.

Data Analysis: Data were analyzed with statistical package for social science (SPSS) version 16. Results were expressed as means, standard deviation and frequencies. The differences in means of CRP between groups and subgroups were compared with students T- test and analysis of variation (ANOVA) as appropriate. P value was set at 0.05.

III. Results

A total of 150 subjects including 120 patient group and 30 controls were recruited. Four subjects in the patient group died before day 8 sample was collected and were thus excluded. Thus 116 patients completed the study. The mean age of trauma patients was 33.75 years and the controls 31.67 years ($P > 0.05$). Table 1 shows the age groups and other demographics of the participants. Forty nine of the patients were withinn the age group of 26 – 35 years representing the modal age group. Ninety four (81.0%) of the patients are males and 63 (54.3%) are singles.

Eighty (69.0%) of the patients had vehicular crashes, 19 (16.4%) had gunshot injuries, 8 (6.9%) had burns injury, 4 (3.4%) each had assault and stab injuries. Fifty nine patients had soft tissue injuries while 57 sustained fracture. Fifteen (12.9%) of the them had surgical intervention among other treatment modalities.

Table 2 and fig. 1 shows the mean and standard deviation of the hsCRP values on days 1, 3 and 8 post injury and those of the controls. hsCRP levels is significantly higher in patient group compared to controls. The value increased significantly by day 3 (peak) and decreased by day 8 though day the 8 value was still higher than day 1. This was the trend in all the injury subtypes except in the patients with burns and assault related injuries as shown in table 3 in whom CRP level continued to increase even on day 8. The changes in the subgroup with assault injuries did not show any significant difference in mean CRP despite the increament.

Comparing CRP levels on each of the days evaluated between the injury subtypes, the mean levels of CRP on days 1 and 3 did not differ significantly between the subgroups but the mean CRP of the patients with stab injuries dropped significantly on day 8 compared to the others as shown in table 4

Based on tissue involvement, CRP levels increased on day 1, peaks at day 3 and declines by day 8 in subjects with soft tissue and bone involvements as shown in table 5. There is no significant difference in the mean level of CRP on each day between those with soft tissue and bone injuries as shown in table 6.

Similarly, the mean CRP significantly increased by day 3 and 8 however the day 8 CRP was lower than day 3 in patients who had surgery as well as those who did not as shown in table 5. CRP levels were significantly higher in the subgroup without surgical intervention on day 1 but the group that had surgery had a significantly higher day 3 CRP as shown on table 6.

IV. Discussion

CRP levels rise in serum or plasma within 24-48hrs following acute tissue damage, peaks during the acute stage and decrease with the resolution of inflammation or trauma.[7] In the index study, we found that CRP levels were significantly higher than controls within 24 hrs of injury, peaked by day 3 and declined by day 8 in all types of physical injuries except in patients with burns and assault related injuries in whom CRP remained persistently high even at day 8.

This marked rise in CRP levels from day 1-3 followed by its decline on day 8, is in keeping with previous studies by Claudia et al[8] and Gupta et al[3]. The maximal generation of CRP on the third day can be linked to high levels of circulating IL-6 release which evidently precedes the equivalent production of CRP by at least 12 hours.[9] This maximal generation of CRP has been described by Ertel et al.[10]

CRP level is known to reflect the impact of trauma on the body and associated tissue damage.[11] The time course of trauma induced CRP production in general goes along with a gap of several hours. As a consequence, elevated CRP levels were more pronounced on the third day irrespective of the degree of tissue damage. However the exception observed in patients who had burns may suggest the presence of infection as a complication. Burns is associated with a high risk of infection due to extensive breakdown of the barrier defence mechanism of the body. Studies by Jeschke et al[12] showed that CRP levels may continue to increase beyond day 8 before it declines though they concluded that CRP may not predict sepsis in burns patients. This observation was corroborated by Pileri et al[13] who showed that CRP increases till day 15 before declining.

When patients with fractures were compared with those who had soft tissue injuries, there was no significant difference in the mean CRP levels in the two groups. This may suggest that CRP response is not dependent on the tissue type involved rather it is the degree of tissue damage that may determine the inflammatory response and therefore CRP levels.[9]

Results from this study showed that CRP levels were higher for patients who had surgery than for those who did not on day 3. It has been reported that CRP rises early after surgical intervention.[14] The rise in CRP after surgical intervention is expected because of tissue injury and associated inflammatory response however persistently elevated CRP may become a biological warning sign, which should raise an index of suspicion for infection.[3]

V. Conclusion

In conclusion, CRP level increases in the blood of trauma patients as a result of tissue damage but decreases after the third day following trauma. However, a sustained increase should be properly investigated as it may suggest complication by infection. We therefore recommend that serial quantitative CRP measurements be done as an adjunct to surgical care in patients with acute injuries.

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2. List of Tables

Table 1: Demographic Parameters of the Study Populace

Variables	Patient Group	Control Group
Age group		
16 – 25	31 (26.7)	7 (23.3)
26 – 35	49 (42.2)	15 (50.0)
36 – 45	20 (17.2)	7 (23.3)
46 – 55	6 (5.2)	1 (3.3)
56 – 65	10 (8.6)	0 (0.0)
Sex		
Male	94 (81.0)	19 (63.3)
Female	22 (19.0)	11 (36.7)
Marital Status		
Single	63 (54.3)	15 (50.0)
Married	53 (45.7)	15 (50.0)
Level of Education		
None	23 (19.8)	
Primary	27 (23.3)	
Secondary	38 (32.8)	
Tertiary	28 (24.1)	

Table 2: Mean ± SD of CRP in Patients and Controls

Variables	Patient Group			Control	P value
	Day 1	Day 3	Day 8		
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
CRP	166.7 ± 105.3**	373.4 ± 131.2**	300.0 ± 156.5**	69.4 ± 68.1	<0.001

Table 3: Changes in CRP based on Injury Subtype

Variables	Freq.(%)	Day 1	Day 3	Day 8	P value
Type of Injury	n=116	Mean ± SD	Mean ± SD	Mean ± SD	
RTA	80 (69.0)	181.6 ± 105.7	365.1 ± 132.9	281.3 ± 154.0	0.001
Gunshot	19 (16.4)	130.4 ± 104.8	422.7 ± 102.1	361.9 ± 157.7	0.001
Burns	8 (6.9)	108.5 ± 84.2	362.9 ± 187.9	424.0 ± 84.6	0.001
Assault	4 (3.4)	196.7 ± 135.6	254.6 ± 74.7	323.9 ± 150.2	0.391
Stab	4 (3.4)	140.7 ± 64.1	416.5 ± 13.0	108.5 ± 40.1	0.001
Grinder	1 (0.9)	118.3	497.8	295.1	NA

Table 4: Comparism of the difference in mean CRP in the subgroups on each study day

Days	Assault	RTA	Gunshot	Burns	Stab	P value
1	196.7 ± 135.6	181.6 ± 105.7	130.4 ± 104.8	108.5 ± 84.2	140.7 ± 64.1	0.144
3	254.6 ± 74.7	365.1 ± 132.9	422.7 ± 102.1	362.9 ± 187.9	416.5 ± 13.0	0.148
8	323.9 ± 150.2	281.3 ± 154.0	361.9 ± 157.7	424.0 ± 84.6	108.5 ± 40.1**	0.003

Table 5: Changes in mean CRP based on tissue involvement and surgical intervention with time

Variables	Freq.(%)	Day 1	Day 3	Day 8	P value
Tissue Involvement					
Soft tissue	59 (50.9)	153.8 ± 106.5	379.5 ± 134.8	301.2 ± 165.5	0.001
Fracture	57 (49.1)	179.3 ± 103.5	367.7 ± 128.5	298.8 ± 148.8	0.001
Surgical Intervention					
Yes	101 (87.1)	116.3 ± 94.2	449.5 ± 45.6	344.3 ± 193.2	0.001
No	15 (12.9)	174.2 ± 105.2	362.2 ±136.0	293.4 ± 150.4	0.001

Table 6: Comparism of changes in CRP on each day based on Tissue Involvement and Surgical Intervention

Days	Soft tissue	Fracture	P value	Surgical Intervention	No Surgical Intervention	P value
	153.8 ± 106.5	179.3 ± 103.5	0.194	116.3 ± 94.2	174.2 ± 105.2**	0.046
	379.5 ± 134.8	367.7 ± 128.5	0.630	449.5 ± 45.6**	362.2 ±136.0	0.015
	301.2 ± 165.5	298.8 ± 148.8	0.936	344.3 ± 193.2	293.4 ± 150.4	0.242

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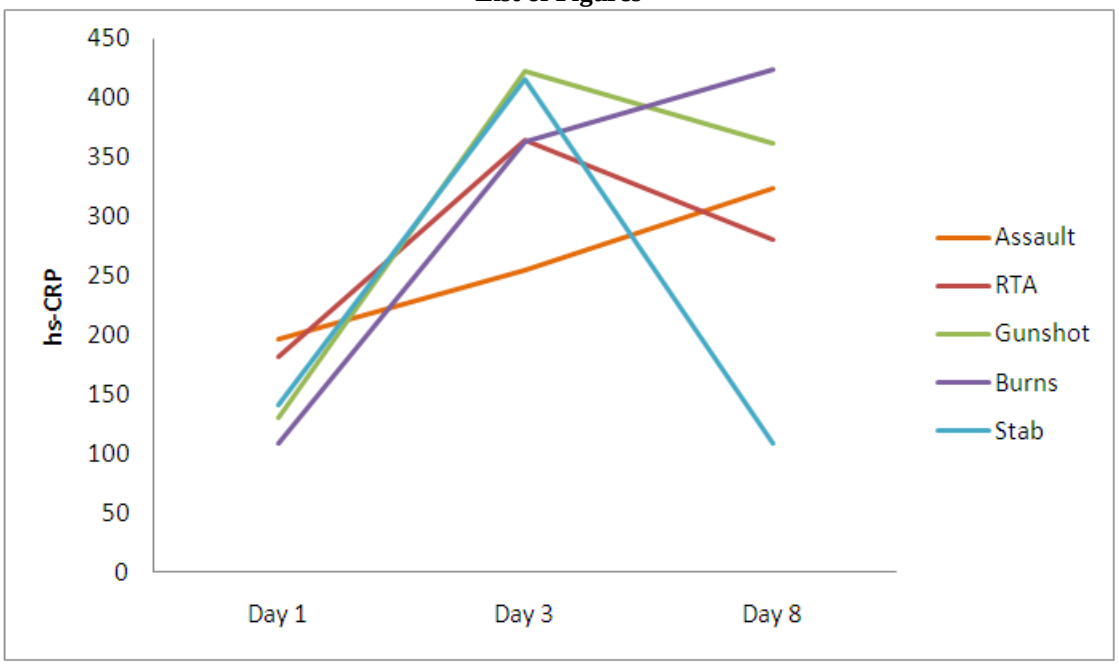

Figure 1: Changes in mean hsCRP levels with time in each subgroup.